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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 09/839,424  | 04/20/2001  | David L. Brown       | 3364/I (PHA 4176)   | 1761             |
| 7590  | 04/20/2005  |                      | EXAMINER            |                  |
| Pharmacia Corporation<br>Corporate Patent Department<br>P.O. Box 5110<br>Chicago, IL 60680-9889 |             |                      | DENTZ, BERNARD I    |                  |
|   |             |                      | ART UNIT            | PAPER NUMBER     |
|   |             |                      | 1625                |                  |

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                        |                     |
|------------------------------|------------------------|---------------------|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |
|                              | 09/839,424             | BROWN ET AL.        |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |
|                              | Bernard Dentz          | 1625                |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 26 November 2004. *(Terminal Disclaimer has been accepted)*
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 7,31,32,35-38,40,41,94,95,101,115-122 and 124-137 is/are pending in the application.
- 4a) Of the above claim(s) 132-137 is/are withdrawn from consideration.
- 5) Claim(s) 22 is/are allowed.
- 6) Claim(s) 7,31,35-38,40,41,94,95,101,115-122 and 124-131 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 9-28-2004 P-1-24-2005
- 4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date: \_\_\_\_\_
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: \_\_\_\_\_

Claims 7,31,32,35-38,40,41,94,95,101,115-122 and 124-131 are rejected under 35 U.S.C. 103(a) as being unpatentable over Merck WO 94/26731 cited by applicants alone, in view of Ando et al, US Patent 6,294,558, Haruta et al, US Patent 6,362,209 and Kimura et al, EP799,823 cited by applicants. The first discloses a relatively small genus of 3- (4-methylsulfonylphenyl or 4-sulfamoyl-phenyl) 4-aryl or hetaryl-thiophenes where the 4-methylsulfonylphenyl and the 4-sulfamoylphenyl groups may be substituted in the 3-position with a halogen selected from fluoro, chloro, bromo or iodine, carboxy or CF<sub>3</sub> as cox-2 inhibitors. When fluoro is selected the instant compounds are covered.

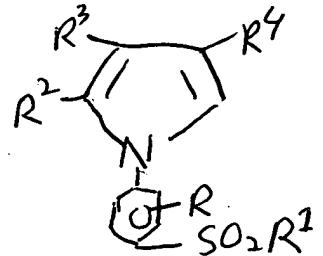
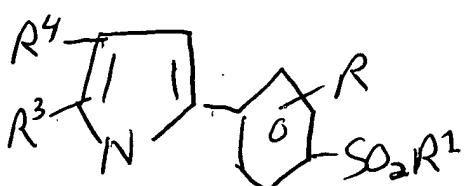
If it could be shown that the later art recognized the particular efficacy of this type of fluoro substitution in this well known group of COX-2 inhibitors then the making of the instant 3-(3-fluoro-4-methylsulfonylphenyl) or 3-(3-fluoro-4-sulfamoylphenyl) 4-aryl or hetaryl thiophenes as COX-2 inhibitors would have been motivated and the instant compounds obvious.

Ando et al shows this for similar compounds differing from the instant compounds in that the 4-aryl moiety is substituted in the 4-position by an aryl group. See col. 9, lines 5-12 and the compounds disclosed at col.12, lines 40-46,51-52,55-58 61 and 65 and col. 13, lines 3-5. However it shows a wide variation for the central aromatic nucleus which is denoted as A therein. Note that A can be the instant thieryl as well as many other hetaryl moieties including pyrrolyl and oxazolyl. Now if one skilled in the art knew that the 3-fluoro-4-methylsulfonyl or 3-fluoro-4-sulfamoyl substitution were preferred in this well known class ofCOX-2 inhibitors not containing

the 4-position aryl substitution on the other aryl substituent then the selection of 3-fluoro-4-methylsulfonyl or 3-fluoro-4-sulfamoyl substitution would have been obvious.

This is shown by Haruta et al for compounds where the central hetaryl moiety is oxazole rather than the instant thiienyl group. It specifically discloses the efficacy of the fluoro group in the instant position at col. 3, lines 37-48.

It is also shown by Kimura et al for pyrroles of the formulae



See pages 1 and 2, the preference of fluoro for R, and p. 9 for the preference of sulfamoyl group for R¹ and Examples 1-161 to 1-166 in Table 1 and Examples 2-152 to 2-160 in Table 2 for the 3-position for fluoro (i.e. ortho the sulfamoyl group).

Thus in view of the above discussion it is readily seen that instant class of 3-(3-F-4-methylsulfonylphenyl or 3-F-4-sulfamoylphenyl)-4-aryl thiophenes as COX-2 inhibitors would have been obvious to one of ordinary skill in the art.

The non-elected material should be cancelled from the claims.

The terminal disclaimer has been accepted.

The 35 USC 112 rejections have been withdrawn.

Applicants should send in sheets 3-8 of the Information Disclosures Statement of Nov. 28, 2001 so that the Examiner may initial the listed references to indicate that they have been considered.

Art Unit: 1625

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bernard Dentz whose telephone number is 571-272-0683. The examiner can normally be reached on Mon-Fri from 8 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on 571 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Dentz

4-11-2005



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